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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,866	05/29/2001	Brian Sorrentino	1340-1-021CIP2	4688

31949 7590 10/20/2004

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,866	SORRENTINO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed 7/29/04 have been entered. Claim 16 has been amended, claims 16, 17, 21-28 are pending in the application and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment and response will not be reiterated. The arguments would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 17, 21-28 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record and following.

In the 7/29/04 response, applicants argue that antibodies have long been described and characterized by those of skill in the art and by the antigens which they recognize, thus it is clear a description of the physical structure of a claimed antibody is not necessary. Applicants go on to cite numerous art of record such as U.S. patent 5,994,088 by Mechetner et al to support such point.

The arguments have been fully considered but found not persuasive. This is because the instant claims are not drawn to just any antibody, but limited to antibodies that recognizes an extracellular portion of a BCRP protein *in its natural conformation*. In the Declaration of Dr. Balzas Sarkadi submitted by the applicants, Dr. Sarkadi indicated that as of the priority date of this application, there was no method known in the art to reliably produce an isolated antibody that recognizes an extracellular portion of the ABC transporter BCRP in a living cell. As such, the claimed antibody does not appear to be conventional in the art, and it is necessary upon applicants to provide an adequate written description to teach the structures of the antibody that allows the recognition of the extracellular portion of the BCRP in its natural conformation. The claims of the cited *Mechetner* patent are not limited to antibodies recognizing the extracellular portion in its natural conformation and method of using such, but encompass methods of using any type of antibody that recognizes a p-glycoprotein, i.e. not necessarily recognizing the extracellular portion in its natural conformation. Thus, granting such patent does not obviate the need for applicants to provide an adequate written description for what is claimed in this application particularly considering that the claims are drawn to a *genus* of antibodies having such capability of recognition of a naturally conformed extracellular portion of BCRP. Likewise, the presence of numerous prior art publications does not obviate the need for applicants to provide an adequate written description for the claimed genus of antibodies because the prior art of record embrace antibodies that would or would not recognize the naturally conformed extracellular portion of BCRP. For example, applicants cited *Scheffer et al* as supporting evidence for the argument, but as

applicants indicated previously, the antibody disclosed by *Scheffer et al* does not recognize the extracellular portion of the BCRP, let alone in its natural conformation.

With respect to the BCRP antigen, Ross et al is the first to disclose the sequence of the BCRP cDNA which encodes the antigen. But applicants have argued and filed affidavit to support that having such antigen and using the same method of production does not reliably produce the antibody that meets claim limitation.

Accordingly, for reasons of record and set forth above, it is appropriate to require a written description for the particular genus of antibodies claimed. Thus, the rejection stands.

Claims 16, 17, 21-28 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In the 7/29/04 response, applicants argue that there are sufficient teachings in the present application for generating the claimed antibodies, and pointing to page 39 of the specification. Applicants go on to argue that in Zhou and Abbott references, several antibodies have been made that recognize an external epitope of the BCRP in its natural conformation using the methodology described in the specification, thus the Office should not doubt the ability of skilled artisans to use the same methodology to generate additional antibodies within the scope of the claims.

The arguments have been fully considered but found not persuasive for reasons of record and following.

It is noted that the method taught in page 39 of the specification (i.e. using a retroviral vector encoding human cDNA to transfect a cell and immunizing mice with the transfected cells) is well known in the art as taught by *Mechetner et al* (see detail under 35 USC § 103 of the previous Office action), but applicants have argued all along, and filed a declaration by a skilled artisan (the Declaration of Dr. Balzas Sarkadi), stating that the art known methods at the time of the invention could not predictably produce the claimed antibody. Apparently, it is the applicants, not the Office, who provide evidence to doubt the enablement of instantly claimed invention.

Applicants go on to argue that the Examiner has not provide rationale for why the detection of BCRP expression in living cells is not sufficient evidence that the antibody made by the applicants recognizes an external epitope of BCRP in its natural conformation. Applicants further raise the question why the Nieman reference cited by the Office is relevant to the enablement rejection.

In response, as an initial matter, the specification fails to disclose whether the antibody produced by the disclosed method had indeed been used in detection of the BCRP expression in living cells. The specification appears to only contemplate such possibility. The *Nieman* reference was cited precisely for providing the rationale as to why the detection of BCRP expression in living cells is not sufficient evidence that the antibody made by the applicants recognizes an external epitope of BCRP in its natural conformation: because an antibody made with a purified protein or a synthetic antibody

is also capable of detecting an extracellular epitope in its natural form as long as it recognizes a part of the epitope. Thus detecting BCRP expression in the living cells does not by itself correlates with the structure of the antibody. As cited previously, *Niman et al* (us 5,563,247) teach that antibody-antigen recognition process is largely conformation-independent, when using a polypeptide (an isolated protein) to produce an antibody, even when the peptide is synthetic, if the amino acid sequence is correspondent to a part of the desired epitope, the produced monoclonal antibodies would react with the intact protein under a variety of reaction conditions "BECAUSE THE RECOGNITION IS LARGELY CONFORMATIONALLY INDEPENDENT" (column 16, lines 9-33, particularly line 27). Accordingly, because the antibody recognition of an antigen is largely conformational independent, and because even a synthetic antibody could recognize an epitope in its natural conformation, an antibody that does not recognize the entire external epitope in its natural conformation can still detects BCRP expression in a living cell. In other words, an antibody could detect an external epitope in its natural conformation as long as it can recognize a part of the entire conformation. Accordingly, based on the unpredictability to make and determine the antibody that meets the claim limitation, it would have required carrying out undue experimentation to determine which of the antibodies would have the recited function and how to reliably producing such. Accordingly, if the prior art fails to teach a method of making such antibodies, so does the specification. Therefore, the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16, 17, 21-28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Ross et al* (US 6,313,277, IDS/AA), in view of *Mechetner et al* (US 5,994,088), for reasons of record and following.

In 7/29/04 response, applicants argue that *Mechetner* does not overcome the general uncertainty in the prior art as indicated in the declaration of Dr. Sarkadi when it comes to the ability to generate antibodies that will recognize the extracellular portion of the ABC transporters even though it describes the generation of an antibody that recognizes an extracellular epitope of the ABC transporter.

In response, the instant specification contemplates the same method as disclosed in the '088 patent (e.g. column 12 of the cited patent), and applicants asserted in the 7/29/04 response that this method would produce antibodies that meet instant claim limitation and citing Zhou and Abbott references as evidence (2nd paragraph, page 11). Applicants are reminded that such evidence further support the position of the Office that with the knowledge of BCRP coding sequence as taught by *Ross et al*, and the known method for producing antibodes recognizing an external epitope of an ABC transporter protein as taught by *Mechetner et al*, a reasonable skilled in the art would have had a reasonable expectation of success for producing an antibody as suggested be *Ross et al*, that could recognize an external epitope of BCRP in its natural

conformation. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See In re O'Farrell, 7 USPQ2d 1673 (CAFC 1988).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the method as taught by *Mechetner et al* in making an antibody that binds to the extracellular epitope of BCRP in its natural conformation with a reasonable expectation of success. Given the methods known in the art, given the knowledge regarding the importance of the extracellular portion of an ABC transporter protein, and given the cDNA of BCRP provided by *Ross et al*, it is within the knowledge of the skilled to make a similar antibody as 4E3 or UIC2 that binds to the naturally conformed extracellular epitope of BCRP as taught by *Mechetner et al*. Thus, the claimed invention as a whole was *prima facie* obvious. Accordingly, the rejection stands.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. Janice Li
Primary Examiner
Art Unit 1632

QL
October 12, 2004